Balanced Cluster Canonical Correlation Analysis for Multimodal Data Integration in Alzheimer's Disease

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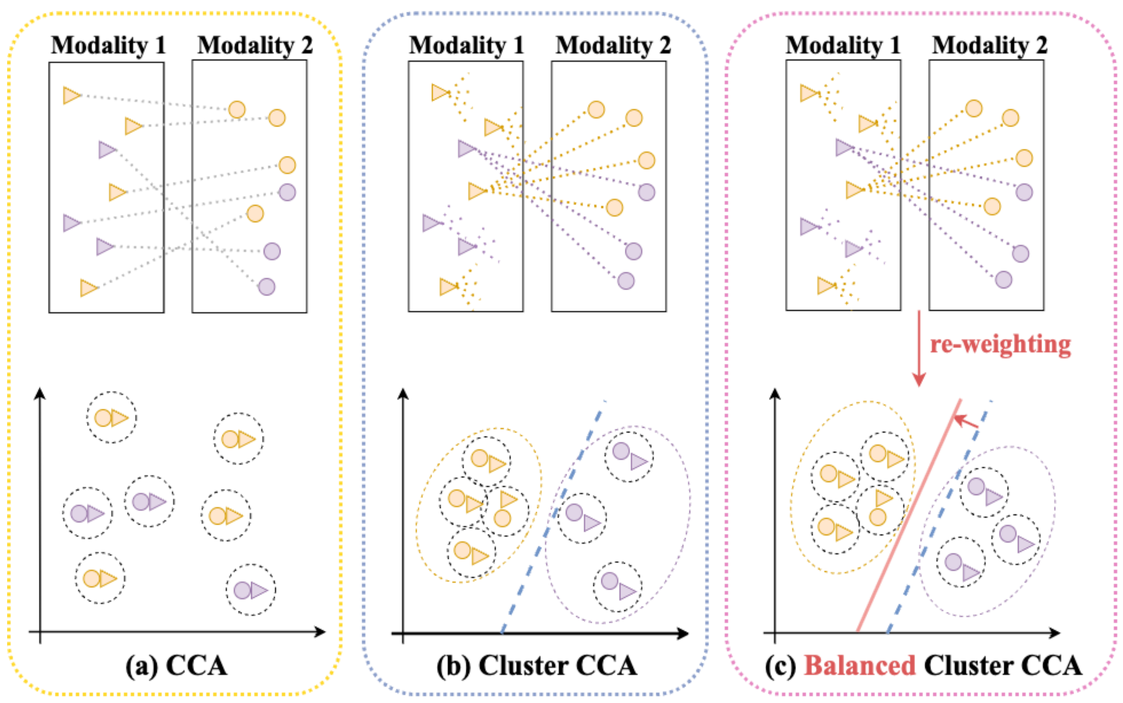
Introduction

- **Canonical Correlation Analysis (CCA)** is a multivariate statistical technique that find linear combinations of variables from two sets that **maximize the correlation** between them, **reveal underlying patterns** and shared structures.
- The applications of CCA span a wide range of fields, each demonstrating its effectiveness in **handling multidimensional data**, especially in Alzheimer's Disease (AD) with multiple imaging modalities or imaging genomics analysis.
- **Problem:** The **label imbalance** in AD cohorts results in the **underrepresentation of minority AD** subjects. Such imbalance skews model learning, producing **biased CCA representations** dominated by the majority group. Consequently, this distortion limits model reliability, delays early diagnosis and precise intervention.
- Existing solutions to imbalance issue including using oversampling or cost-sensitive learning in combination with CCA. However, they will modify the original data distribution or rely on adjustments in subsequent classification models.
- **Goal:** propose an approach that **directly learns a balanced representation** within CCA for the class imbalanced dataset.

Methods



$$\max_{\mathbf{U},\mathbf{V}} \ \text{trace}\left(\mathbf{U}^\top \mathbf{X}^\top \mathbf{Y}\mathbf{V}\right)$$
$$\text{subject to} \quad \mathbf{U}^\top \mathbf{X}^\top \mathbf{X}\mathbf{U} = \mathbf{V}^\top \mathbf{Y}^\top \mathbf{Y}\mathbf{V} = \mathbf{I}_r.$$

Traditional CCA identifies **pairwise correspondences**.

$$\max \ \text{trace}\left(\mathbf{U}^\top \bar{\mathbf{\Sigma}}_{\mathbf{xy}} \mathbf{V}\right)$$
$$\text{subject to} \quad \mathbf{U}^\top \bar{\mathbf{\Sigma}}_{\mathbf{xx}} \mathbf{U} = \mathbf{V}^\top \bar{\mathbf{\Sigma}}_{\mathbf{yy}} \mathbf{V} = \mathbf{I}_r,$$

Cluster CCA enhances **within-class correspondences**, improving class **separability**.

$$\bar{\mathbf{\Sigma}}_{\mathbf{xx}} := \frac{1}{\sum_{c=1}^{C} |\mathbf{X}^c||\mathbf{Y}^c|} \sum_{c=1}^{C} \frac{\sum_{c'=1}^{C} n_{c'}}{n_c} \sum_{j=1}^{|\mathbf{X}^c|} |\mathbf{Y}^c| \mathbf{x}_j^{c\top} \mathbf{x}_j^c,$$
$$\bar{\mathbf{\Sigma}}_{\mathbf{yy}} := \frac{1}{\sum_{c=1}^{C} |\mathbf{X}^c||\mathbf{Y}^c|} \sum_{c=1}^{C} \frac{\sum_{c'=1}^{C} n_{c'}}{n_c} \sum_{k=1}^{|\mathbf{Y}^c|} |\mathbf{X}^c| \mathbf{y}_k^{c\top} \mathbf{y}_k^c,$$
$$\bar{\mathbf{\Sigma}}_{\mathbf{xy}} := \frac{1}{\sum_{c=1}^{C} |\mathbf{X}^c||\mathbf{Y}^c|} \sum_{c=1}^{C} \frac{\sum_{c'=1}^{C} n_{c'}}{n_c} \sum_{j=1}^{|\mathbf{X}^c|} \sum_{k=1}^{|\mathbf{Y}^c|} \mathbf{x}_j^{c\top} \mathbf{y}_k^c.$$

Balanced Cluster CCA employs **re-weighting** to further **balance the representations** of two classes, widening the **margin for minority** classes.

ADSP Data

Modality	# features	Diagnosis Distribution	Canonical Dimension
MRI Volume	151	977 CN, 512 MCI, 322 AD	10
SNPs	1789		

- 1,811 subjects from multiple cohorts with their first visit (ADRC, WHICAP, WRAP, and ADNI at the R4 phase)
- Binary classifications: CN vs. AD, CN vs. MCI and MCI vs. AD
- Models:
  - CCA, Cluster CCA, Balanced Cluster CCA
  - CCA models + SVM, original data + SVM

Results

❖ AD Classification Performance with ADSP data

- For the **high-dimensional** ADSP data, even the **traditional CCA+SVM** method achieves **better** predictive performance than **directly applying SVM** to the original data, highlighting the advantage of CCA in handling high-dimensional data.
- Our proposed **Balanced Cluster CCA** consistently achieves the **highest balanced accuracy** across all classification tasks, demonstrating its effectiveness in representing imbalanced-label data and improving classification performance in Alzheimer's disease studies.

ADSP IMAGE AND SNPS DATASETS.

Methods	CN vs. AD		CN vs. MCI		MCI vs. AD	
	BACC	ACC	**BACC**	ACC	**BACC**	ACC
SVM	0.784±0.041	0.850±0.026	0.651±0.017	0.704±0.020	0.740±0.020	0.759±0.015
CCA+SVM	0.797±0.029	0.872±0.019	0.676±0.039	0.729±0.032	0.764±0.029	0.784±0.022
C-CCA+SVM	0.821±0.011	0.888±0.011	0.703±0.046	0.739±0.045	0.751±0.042	0.777±0.034
BC-CCA+SVM	**0.841±0.014**	0.894±0.010	**0.730±0.018**	0.761±0.015	**0.778±0.038**	0.796±0.030

Discussion

- Produces **balanced** cluster densities in the low-dimensional **representations** by tightening minority class representation, relaxing compactness in majority class, and enhances between-class separation
- **Future directions:**
  - Develop non-linear extensions
  - Integrate other multi-view learning approaches
  - Broader downstream tasks across various fields and datasets

Conclusion

The Balanced Cluster CCA effectively **addresses class imbalance** in Alzheimer's disease research through reweighting. It **outperforms standard CCA** methods in classification tasks and shows strong potential for broader biomedical applications involving imbalanced data.

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